In the Claims:

The presently pending claims are as follows:

64

1 (Once Amended). A method for stimulating angiogenesis within a targeted collection of viable cells in-situ, said method comprising the steps of:

identifying a collection of cells comprising viable cells in-situ as a target for stimulation of angiogenesis;

providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;

introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using said effecting means;

allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby

(a) some of the proteasomes can interact directly with said PR-39 oligopeptide collective member while other proteasomes can interact indirectly with said PR-39 oligopeptide collective member, and

(b) the proteolytic degradation of at least one identifiable peptide mediated by said interacting proteasomes becomes altered while the proteolytic degradation mediated by said interacting proteasomes against other individual peptides remains unaltered, and

(c) the altered proteolytic degradation of said interacting proteasomes results in a stimulation of angiogenesis in-situ within the targeted collection of viable cells.

2 (Once Amended). A method for altering proteasome-mediated degradation of peptides in-situ within a collection of viable cells, said method comprising the steps of:

By Conclude

identifying a collection of cells comprising viable cells in-situ as a target;

providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;

introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using effecting means;

allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby

(a) some of the proteasomes can interact directly with the PR-39 oligopeptide collective member while other proteasomes can interact indirectly with said PR-39 oligopeptide collective member, and

(b) the proteolytic degradation of at least one identifiable peptide mediated by said interacting proteasomes becomes markedly altered while the proteolytic degradation mediated by said interacting proteasomes against other individual peptides remains unaltered, and

(c) the markedly altered proteolytic degradation of said interacting proteasomes results in an increased expression of said identifiable peptide in-situ within the targeted collection of cells.

3. The method as recited in claim 1 or 2 wherein said collection of viable cells includes at least one type of cell selected from the group consisting of endothelial cells,

myocytes and myoblasts, fibrocytes and fibroblasts, epithelial cells, osteocytes and osteoblasts, neuronal cells and glial cells, erythrocyctes, leukocytes, and progenitor cells of all types.

4. The method as recited in claim 1 or 2 wherein said collection of cells comprises at least one tissue selected from the group consisting of myocardium, skeletal muscle, smooth muscle, an artery, a vein, lung, brain, kidney, spleen, liver, gastrointestinal tissue, nerve tissue, limbs, and extremities.

B5

5 (Once Amended). The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member include one selected from the group consisting of catheter-based means, injection-based means, infusion-based means, localized intravascular means, liposome-based means, receptor-specific peptide means, and slow releasing means for peptide secretion in living cells and sequested organisms.

6 (Once Amended). The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member includes DNA sequences coding for at least one PR-39 oligopeptide collective member in an expression vector for transfection and subsequent expression of the PR-39 oligopeptide collective member within said cells.

7. The method as recited in claim 1 or 2 wherein said method is practiced under in-vivo conditions.

8. The method as recited in claim 1 or 2 wherein said method is practiced under in-vitro conditions.

9 (Once Amended). The method as recited in claim 1 or 2 wherein degradation of 1Kβα is inhibited.

10 (Once Amended). The method as recited in claim 1 or 2 wherein degradation of HIF- 1α is inhibited.

11 (Once Amended). A family of PR-39 derived oligopeptides whose members individually cause an alteration in proteasome-mediated degradation of at least one identifiable peptide in-situ after introduction intracellularly to a viable cell, each member of said PR-39 derived oligopeptide family

being a peptide less than 26 amino acid residues in length;

having a N-terminal amino acid residue sequence which begins with Arg-Arg-Arg;

is a peptide devoid of the amino acid residue sequences Pro-Pro-X-X-Pro-Pro-X-X-Pro and Pro-Pro-X-X-X-Pro-Pro-X-X-Pro where X is any amino acid;

is able to interact in-situ with such proteasomes as are present within the cytoplasm of the cell; and

is able to alter markedly the proteolytic degradation of at least one identifiable peptide mediated by said interacting proteasomes such that an increased expression of said identifiable peptide occurs in-situ.

12. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 15 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-Arg-Pro-Pro.

13. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 11 amino acids residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg.

14. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 8 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr.

REMARKS

The Examiner has objected to the Specification regarding the content of original pages 13, 20, and 28 respectively. In addition, the Examiner has rejected the original claims under 35 U.S.C. 112, second paragraph as being indefinite in language for specifically stated reasons. Finally, the Examiner has rejected the claims under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 5, 654, 273. In response, applicants have amended the Specification; added new Figs. 8-10 respectively; and amended original claims 1-2. 5-6 and 9-11 respectively. By these amendments, applicants believe they have overcome and obviated each basis for objection and rejection stated by the Examiner in the instant first Official Action.